Total Parenteral Nutrition for Neonates

1. Introduction
   - Total parenteral nutrition (TPN) is the intravenous infusion of all nutrients necessary for metabolic requirements and growth
   - The earlier introduction and more aggressive advancement of TPN was shown to be safe and effective, even in the smallest and most immature infants.
   - Premature infants tolerate TPN from day 1 of post-natal life.

The goal of TPN is to:
   - provide sufficient nutrients to prevent negative energy and nitrogen balance and essential fatty acid deficiency
   - support normal rates growth without increased significant morbidity.

Indication for TPN:
   - gastrointestinal tract abnormalities (omphalocele, gastroschisis, Tracheo-esophageal fistula, malrotation with volvulus, etc).
   - necrotizing enterocolitis (NEC),
   - respiratory distress syndrome / BPD patients who are unable to tolerate feedings
   - extreme prematurity,
   - sepsis,
   - malabsorption.

2. Components of TPN

The essential components of parenteral nutrition are:
   - fluids;
   - carbohydrate;
   - electrolytes;
   - protein;
   - lipids;
   - vitamins; and
   - trace minerals.

When a baby is on parenteral nutrition, our ultimate goal is to provide at least 100-110 cal/kg/day. This will be achieved if we can deliver (for example) 150 cc/kg/day of 12.5% dextrose, 2.5 g/kg/day of synthetic amino acids, and 3.0 g/kg/day of intravenous lipids.

2.1 Fluid
   - Fluid is an essential component of parenteral nutrition.
   - Fluids are usually started at 80-100 ml/kg/day (if newborn), or at whatever stable fluid intake the baby is already receiving.
   - Volumes are increased over the first 7 days in line with the fluids and electrolytes protocol with the aim to deliver 150 ml/kg/day by day 7.

2.2 Amino acids
   - Amino acids prevents catabolism
   - Prompt introduction of amino-acids via TPN achieves an early positive nitrogen balance for the infant
- It also decreases the frequency and severity of neonatal hyperglycaemia by stimulating endogenous insulin secretion and stimulating growth by enhancing the secretion of insulin and insulin-like growth factors.
- Protein is usually started at 1g/kg/day of crystalline amino acids and subsequently advanced, by 3rd to 4th postnatal day, to 3.0 g/kg/day of protein in term and 3.7 to 4.0 g/kg/day in the extremely low birthweight (ELBW) infants.
- Reduction in dosage may be needed in critically ill, significant hypoxaemia, suspected or proven infection and high dose steroids.
- Adverse effects of excess protein include a rise in urea and ammonia and high levels of potentially toxic amino acids such as phenylalanine.

### 2.3 Glucose

- There is a relatively high energy requirement in the ELBW because of relatively large body proportion of metabolically active organs i.e. head, liver, kidney, and brain and a large and continuous source of glucose is required for energy metabolism.
- In the ELBW minimum supply rate is 6 mg/kg/min to maintain adequate energy for the brain and an additional 25 cal/kg or 2-3 mg/kg/min of glucose per gram of protein intake is necessary to support protein deposition. The maximum rate is 12 to 13 mg/kg/min (lower if lipid is administered concurrently) but in practice glucose administration is often limited by development of hyperglycaemia which is reported in 20-80% of ELBW infants. This is attributed to peripheral and hepatic insulin resistance presumably due to glucagon, catecholamine and cortisol release and decreased insulin secretion.
- Strategies for the management of hyperglycaemia in the ELBW include decreasing glucose administration, administering intravenous amino acids (which increases insulin secretion) and infusing exogenous insulin infusion.
- Glucose administration is usually initiated at 6 mg/kg/min advancing to 10 to 12 mg/kg/min. If hyperglycaemia develops glucose infusion is decreased and if it still occurs at 3 to 4 mg/kg/min insulin is started.

### 2.4 Lipid

- This is the most controversial of the major intravenous substrate. It is needed to prevent essential fatty acid deficiency, serve as energy substrate and improve delivery of fat soluble vitamins.
- LBW infants may have immature mechanisms for fat metabolism. A number of clinical conditions inhibit lipid clearance e.g. infection, stress and malnutrition.
- Lipid is usually started at 1g/kg/day and this is gradually increased to a limit of 3 g/kg/day (sometimes up to 3.5g/kg/day in the ELBW)
- It is infused continuously over as much of the 24 hour period as practical and smaller doses are used in patients with infection, compromised pulmonary function or hyperbilirubinemia.
- Enzymes responsible for lipid clearance are lipoprotein lipase, hepatic lipase, and lecithin cholesterol acyltransferase. Activation of enzymes can be induced with the administration of low-dose heparin.
Clearance is usually monitored by measuring plasma triglyceride levels. Maximal plasma triglyceride (TG) concentration ranges from 150 mg/dl to 200 mg/dl. It has been suggested that exogenous lipid interferes with respiratory function. Suggested mechanisms include impaired gas exchange from pulmonary intravascular accumulation or impaired lymph drainage resulting in oedema. There are reports of increased pulmonary vascular resistance of a dose and time dependent nature which suggest lipid may aggravate pulmonary hypertension in susceptible individuals.

2.5 Electrolytes
- The usual sodium need of the newborn infant is 2-3 mEq/kg/day in the term and 4-5 mEq/kg/day in the preterm.
- Potassium needs are 2-3 mEq/kg/day in both term and preterm infants.

2.6 Minerals, Calcium (Ca), Phosphorus (P) And Magnesium
- Presently the premature infant is by no way able to maintain the intrauterine accretion rate of Ca and P when parenterally fed.
- Several methods to prevent precipitation of dibasic calcium phosphate in PN solutions have been proposed to circumvent this but until now the optimal retention of calcium and phosphate remains limited to half of the intrauterine accretion.
- Monitoring for osteopaenia of prematurity is important especially when PN is given for prolonged periods.
- A normal magnesium level is a prerequisite for a normal calcaemia. In well balanced formulations, however, magnesium does not give rise to major problems.

2.7 Trace Elements
Is indicated if PN is administered for more than 1 week or longer. Commercial preparations for paediatric use are available.

2.8 Vitamins
Both fat and water soluble vitamins are essential. It should be added to the fat infusion instead of amino-acid glucose mixture to reduce loss during administration

3. Administration
- TPN should be delivered where possible through central lines.
- Peripheral lines are only suitable for TPN of less than 3 days duration and dextrose concentration of less than 12.5%.
- Peripheral lines is also limited by the osmolality (not more than 600 mOsm/L) of solutions that can be used to prevent phlebitis.
- Usually a percutaneous central line is placed with the position of the tip of the catheter confirmed on x-ray prior to use.
- A strict aseptic technique in preparation and administration of the TPN is essential.
- Ideally, breakage of the central line through which the TPN is infused should be avoided, though compatible drugs can be administered if necessary.
Cautions

- **Hyperkalaemia.** Addition of potassium is rarely required in first three days of life unless the serum potassium is < 4.00 mmol/l. Also use caution when prescribing in renal impairment. A minimal amount is inevitable in TPN because of the type of amino acid formulation used.
- **Hypocalcaemia.** May result from inadvertent use of excess phosphate. Corrects with reduction of phosphate.
- **NEVER add bicarbonate,** it will precipitate calcium carbonate out.
- **NEVER add extra calcium** to the burette, it will precipitate out the phosphate.

4. Complications

4.1. Delivery
The line delivering the TPN may be compromised by:
- **Sepsis,** minimized by maintaining strict sterility of the line during and after insertion.
- **Malposition,** x-ray mandatory before infusion commences.
- **Thrombophlebitis,** with peripheral lines, requiring close observation of infusion sites.
- **Extravasation** into the soft tissue, with resulting tissue necrosis.

4.2. Metabolic complications
- Hyperglycaemia
- Hyperlipidaemia
- Cholestasis

5. Monitoring
TPN administration requires careful clinical and laboratory monitoring
Before starting an infant on parenteral nutrition, investigation required:
- full blood count /haematocrit,
- renal profile
- liver function test
- random blood sugar/dextrostix
- serum bilirubin

While on TPN, monitoring required:

5.1. Laboratory
- Full blood count, renal profile.
  Required daily for 1 week then 3 times a week
- Plasma calcium, magnesium, and phosphate.
  Twice a week until stable then weekly
- Lipid levels.
  Twice a week first week then weekly unless complication arises (sepsis etc)
- Long term TPN (> 2 weeks duration) requires, liver function tests.

5.2 Clinical
- Blood sugar / dextrostix, 4-6 hrly first 3 days, twice a day once stable.
- Daily weight
- Meticulous care of the catheter site and monitoring of infection.

This protocol is adapted from:

1. Feeding in the Neonatal Unit
   
   Dato Dr. Lim Nyok Ling, Consultant Neonatologist, Hospital Selayang.

2. Total Parenteral Nutrition for Neonates.
   
   Department of Neonatal Medicine Protocol Book
   Royal Prince Alfred Hospital.

3. Total Parenteral Nutrition for Premature Infants
   
   Elizabeth Brine, MMSc, RD; Judith A. Ernst, DMSc, RD

4. Neonatology on the Web
   
   Teaching Files: Parenteral Nutrition (PN) for Neonate
   Ray Duncan, MD, Staff Neonatologist, Cedars-Sinai Medical Center, Los Angeles, California.